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NEWS

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THEORY HELPS EXPLAIN CANCER GROWTH

A space scientist has devised and demonstrated a theory that helps to explain the source of uncontrolled malignant growth and indicates short cuts to the development of chemical countermeasures against cancer.

The scientist is Clarence D. Cone, Jr., head of the National Aeronautics and Space Administration's Molecular Biophysics Laboratory at NASA's Langley Research Center, Hampton, Va. He specializes in the investigation of space radiation effects on the blockage of cell division.

Cone described his new theory on cell division to the 12th Annual Science Writers Seminar of the American Cancer Society today in San Antonio, Texas. This is the second year in a row that Cone has been invited by the society to tell the science writers about one of his research accomplishments.

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Cone's paper, "Control of Cell Division by the Electrical Voltage of the Surface Membrane," explained his theory and told how it had been experimentally verified in Langley laboratory tests.

The Cone theory proposes that the division of body cells (a normal process that goes on continuously), is controlled precisely by the pattern of ion concentrations on the surface tissues of cells. The pattern is formed by the electrical voltage that normally exists across cellular surfaces and varies from one part of the body to another.

This theory has provided, possibly for the first time, an explanation of the functional connection between the two major pathological features of cancer -- uncontrolled growth of cells and the spread of the disease in the body.

Cone said the theory implies that the basic functional aberrancy -- deviation from normalcy -- producing both of these conditions lies in an alteration of the molecular structure of the cell surface.

Cone explained the electrical aspect by detailing recent Langley studies concerned with space radiation blockage of cell division.

In that research, he noticed that cells having large negative membrane voltages seldom if ever divide while cells with small negative electrical potential divide at maximum rates.

This led Cone to propose the theory that the cellular ionic concentrations, which generate electrical voltage, determine whether or not a cell will divide. A comprehensive experimental test revealed that ion concentration differences between membranes did indeed exert a powerful control over cell division.

The Cone theory proposes a central mechanism for control of body cell division, which, if it proves to be generally valid, will provide a powerful new basis for research progress on many key biomedical problems, such as human conception, birth defects, growth, aging and particularly, cancer.

"In essence," Cone observed, "it explains the fundamental source of the uncontrolled growth of malignancy, knowledge of which should lead to a number of new approaches to cancer control."

The deadliness of cancer arises from two abnormalities characteristic of all malignant cells: their uncontrolled proliferation and their ability to metastasize -- spread to other parts of the body -- and invade normal surrounding tissues.

Previously, there has been no known relationship between these two characteristics, although they always occur together. Cone's theory and experimental observations on the electrical voltage-level control of cell division imply that these two properties of cancer cells are intimately related.

A fundamental implication of Cone's research is that the primary change which occurs when a normal cell is transformed to a malignant one consists of a basic functional change in the molecular architecture and special characteristics of the cell surface.

This surface abnormality accounts for two primary features of cancer: the decreased adhesiveness of the cells (allowing them to invade and spread) and the lowered electrical voltage level which permits the unrestrained growth.

The changes in molecular characteristics which accompany malignant transformation produce what may be descriptively termed "molecular amnesia" of the surface; the malignant cells are thus unable to recognize and relate to their environment of normal and/or other malignant cells. The cells seem to "think" molecularly that they are in a semidissociated state approaching that of tissue culture.

The step-by-step theory of Cone proposes (1) that metabolically induced and stabilized cell surface polymer (molecular structure) alterations play the central role in malignancy, (2) those changes cause decreased surface adhesion and lowered electrical voltage levels with attendant metastasis and active proliferation; and (3) the lowered voltage level then feeds back to stabilize and sustain the very metabolic pathways which act to produce it.

If the Cone concepts are generally valid, the implications for cancer control are significant, for attention is now focused on a specific component of the cell, the surface complex, and on a particular aspect of metabolism -- that concerned with surface polymer production and assembly.

Cone sees the need for a greatly increased understanding of the cell surface complex, leading to possible new methods of attack on malignancy.

The scientist suggested a short cut in the complex study of the metabolic pathway alterations which ultimately lead to surface abnormalities in malignant cells. By studying cancer viruses which have only four or five genes, it should be possible, he said, to determine which genes are producing what surface abnormalities and even to map the associated metabolic changes which take place in the course of malignant transformation.

Once the specific surface abnormalities are identified, they can then be looked for in other forms of cancer, and chemical countermeasures to their malfunctive properties can be developed.

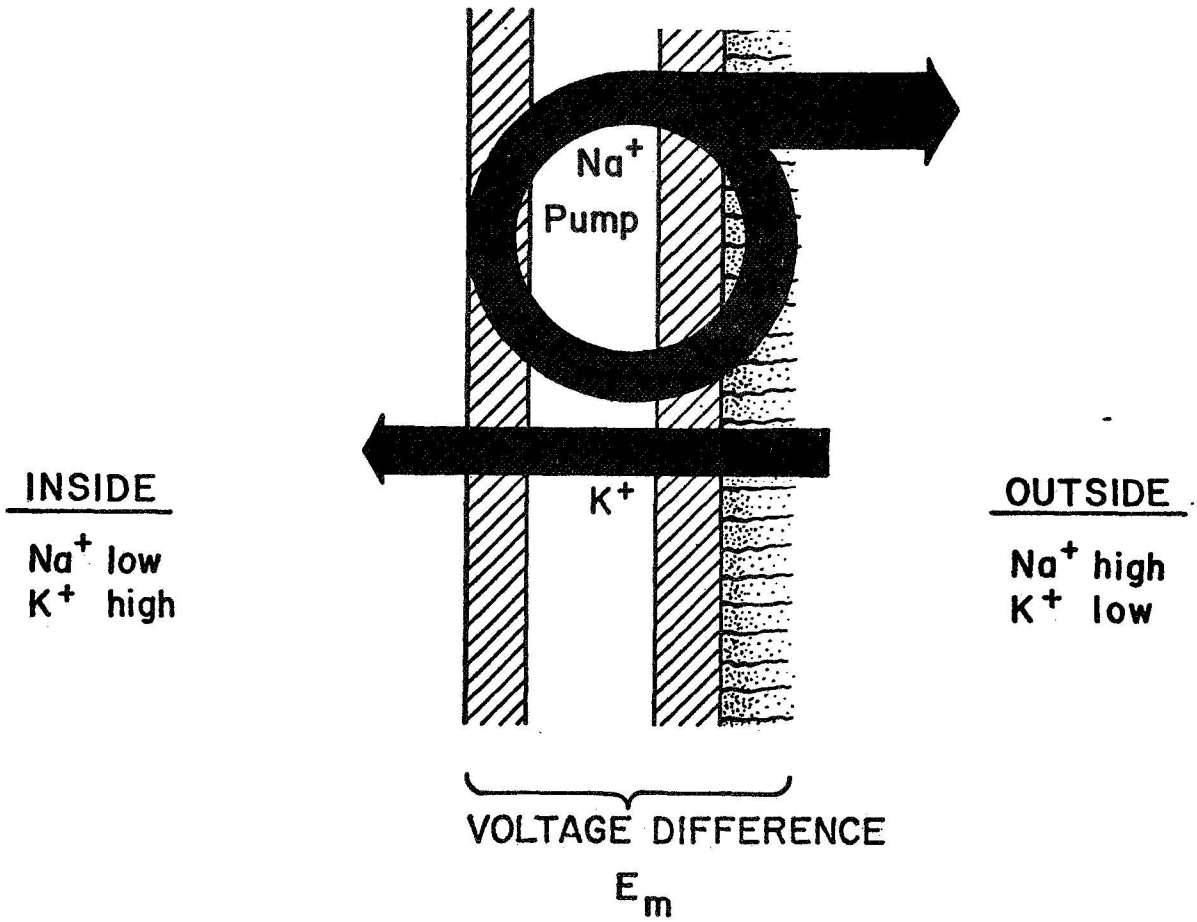
In 1969, Cone, 38, reported the discovery of intercellular bridges that may help in understanding the behavior of certain types of cancer. This previous discovery by Cone has been serving as the basis for further study by scientists to determine if these cell linkages exist in, and possibly constitute the basic cause of uncontrolled proliferation in any types of human cancer of primary medical importance.

Cone's scientific contributions to the solution of the cancer problem are spinoffs from his basic investigations in the field of space radiation.

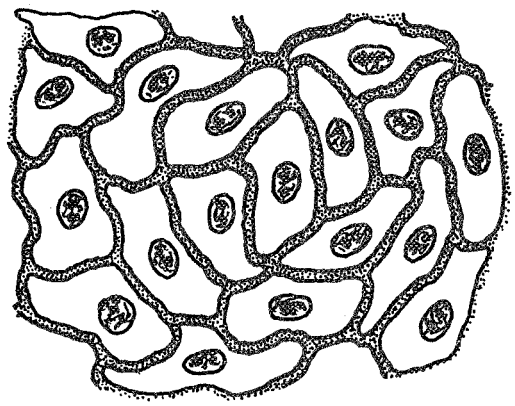
Basically a chemical engineer (Georgia Institute of Technology), Cone also has a Master's degree in aeronautical engineering (University of Virginia).

In addition to his molecular level studies in cellular biophysics, Cone has engaged in research on various aspects of avian biophysics and natural aerodynamics, particularly the aerodynamic theory of soaring and flapping birdflight on which he is an international authority.

Cone, a native of Savannah, Ga., joined the Langley staff in 1956. He lives in Yorktown, Va.

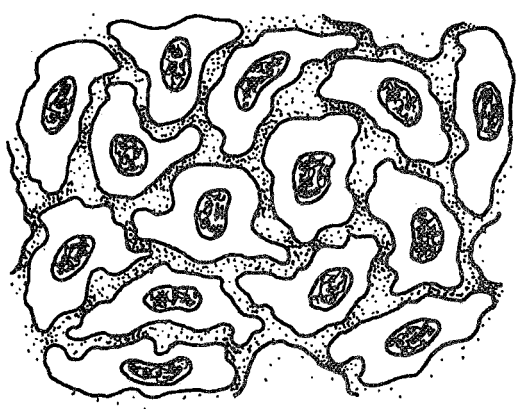


Each normal cell of the human body possesses a surprising degree of negative electrical charge produced by active pumping of positive sodium ions out of the cell. This removal of sodium ions generates a substantial electrical voltage (E_m) across the surface membrane; this voltage can be accurately measured by inserting ultramicro electrodes into the cell, and serves as a convenient indication of the degree to which the ionic concentrations, primarily those of sodium (Na^+) and potassium (K^+), differ between the inside and outside of the cell.



NORMAL CELLS

1. Cell surface bonding strong.
2. Cells remain in place.
3. Electrical voltage level high.
4. Cells divide at low rate.



MALIGNANT CELLS

1. Cell surface bonding very weak.
2. Cells mobile, spread and invade normal tissue.
3. Electrical voltage level low.
4. Cells divide at rapid pace.